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International Application No.: **PCT/US03/10840**  
International Filing Date : **09 April 2003**  
Title : **Oligomeric Compounds Having Modified  
Phosphate Groups**  
Applicant : **Isis Pharmaceuticals, Inc.**

**LETTER ACCOMPANYING AMENDMENT AND  
STATEMENT UNDER PCT ARTICLE 19**

International Bureau of WIPO  
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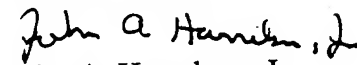
Dear Sir, Madam:

In response to the International Search Report mailed 10 September 2004, for the above-identified International Patent Application, enclosed is an Amendment Under Article 19. Sheets numbered 96 and 99 are enclosed to replace originally submitted sheets 96 and 99 of the claims.

Claims 1 and 24 are amended in the replacement sheets. The basis for the amendments can be found, for example, at page 10, lines 5-7 of the paragraph immediately above paragraph 26.

An edited version of the originally submitted claims is attached and shows the changes that have been made to the claims.

Respectfully submitted,



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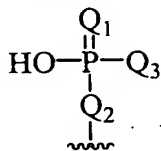
oligonucleotide, an oligonucleoside or said modified phosphate group;

each  $X_1$  and  $X_2$  is, independently, O or S wherein at least one  $X_1$  is S;

$n$  is from 3 to 48; and

wherein at least one of  $J_1$ ,  $J_2$ ,  $J_3$ ,  $T_1$  or  $T_2$  is said modified phosphate group.

2. The oligomeric compound of claim 1 wherein  $Q_1$  is S.
3. The oligomeric compound of claim 1 wherein  $Q_2$  is S.
4. The oligomeric compound of claim 1 wherein  $Q_3$  is  $CH_3$ .
5. The oligomeric compound of claim 1 wherein  $J_1$  is said modified phosphate group.
6. The oligomeric compound of claim 1 wherein at least one  $J_2$  is said modified phosphate group.
7. The oligomeric compound of claim 1 wherein  $J_3$  is said modified phosphate group.
8. The oligomeric compound of claim 1 wherein  $R_1$  is a modified phosphate group.
9. The oligomeric compound of claim 1 wherein at least one  $R_2$  is a modified phosphate group.
10. The oligomeric compound of claim 1 wherein  $R_3$  is a modified phosphate group.
11. The oligomeric compound of claim 1 wherein  $R_1$ ,  $R_3$  and each  $R_2$  is



wherein

one of Q<sub>1</sub> and Q<sub>2</sub> is S and the other of Q<sub>1</sub> and Q<sub>2</sub> is O;

Q<sub>3</sub> is OH or CH<sub>3</sub>;

R<sub>1</sub>, R<sub>3</sub> and each R<sub>2</sub> is, independently, hydrogen, hydroxyl, a sugar substituent group, or a protected sugar substituent group or a phosphorthioate monoester;

each X<sub>1</sub> and X<sub>2</sub> is, independently, O or S wherein at least one X<sub>1</sub> is S; and  
n is from 3 to 48;

wherein at least one of X<sub>1</sub>, X<sub>2</sub>, J<sub>1</sub>, J<sub>2</sub>, and J<sub>3</sub> is said modified phosphate group.

25. The oligomeric compound of claim 24 wherein Q<sub>1</sub> is S.
26. The oligomeric compound of claim 24 wherein Q<sub>2</sub> is S.
27. The oligomeric compound of claim 24 wherein Q<sub>3</sub> is CH<sub>3</sub>.
28. The oligomeric compound of claim 24 wherein J<sub>1</sub> is said modified phosphate group.
29. The oligomeric compound of claim 24 wherein at least one J<sub>2</sub> is said modified phosphate group.
30. The oligomeric compound of claim 24 wherein J<sub>3</sub> is said modified phosphate group.
31. The oligomeric compound of claim 24 wherein R<sub>1</sub> is a modified phosphate group.
32. The oligomeric compound of claim 24 wherein at least one R<sub>2</sub> is a